

IN THE CLAIMS:

1. Canceled.

2. (Thrice amended) A ~~gene delivery vehicle~~ recombinant adenovirus with a significantly reduced tissue tropism for liver cells.

3-18. Canceled.

19. (Four times amended) A cell for producing a ~~gene delivery vehicle~~ recombinant adenovirus having a tissue tropism for smooth muscle cells, said cell comprising:

means for ~~the assembly of gene delivery vectors~~ assembling said recombinant adenovirus;

wherein said means includes at least one ~~adenovirus~~ adenoviral nucleic acid ~~for the production of~~ encoding an adenoviral fiber protein, ~~wherein said adenoviral fiber protein comprises~~ having at least a tissue tropism determining fragment of a subgroup B adenoviral fiber protein; and

wherein said cell is of PER.C6 (ECACC deposit number 96022940) origin.

20. Canceled.

21. (Twice amended) A pharmaceutical composition comprising:
the ~~gene delivery vehicle~~ recombinant adenovirus of claim 1 2; and ~~together with~~
a suitable vehicle.


22-24. Canceled.

25. (Four times amended) An adenovirus capsid with a significantly reduced tissue tropism for liver cells ~~wherein said adenovirus capsid comprises~~ comprising:
proteins from at least two different adenoviruses; and
wherein at least one of the proteins includes at least a tissue tropism determining fragment of a fiber protein is of subgroup B adenovirus origin.

26-27. Canceled.

28. (Twice amended) A construct deposited with the ECACC under deposit number 01121708 ~~on December 12, 2001.~~

29. (Twice amended) A construct deposited with the ECACC under deposit number 01121710 ~~on December 12, 2001.~~

 30. (Twice amended) A construct deposited with the ECACC under deposit number 01121709 ~~on December 12, 2001.~~

31. (Twice amended) A construct deposited with the ECACC under deposit number 01121711 ~~on December 12, 2001.~~

32. (Twice amended) A construct deposited with the ECACC under deposit number 0112712 ~~on December 12, 2001.~~

33-36. Canceled

37. (Four times amended) A method ~~of~~ for reducing ~~an adenovirus capsid~~ of a tissue tropism of an adenovirus capsid for liver cells, said method comprising: ~~incorporating a fragment of a fiber protein of adenovirus 16 in an adenovirus capsid therefor.~~

i) exchanging a first nucleic acid encoding a tissue-tropism determining fragment of a fiber protein for a second nucleic acid encoding a tissue-tropism determining fragment of a fiber protein of adenovirus 16;

ii) introducing the resulting nucleic acid from step i) into a cell capable of producing said adenovirus capsid; and

iii) allowing said cell to produce said adenovirus capsid.

38. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 2, wherein said reduced tissue tropism is ~~being~~ provided by a virus capsid.

39. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 38, wherein said virus capsid comprises protein fragments from at least two different viruses.

40. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 39, wherein at least one of said at least two different viruses is an adenovirus.

41. Canceled.

42. (Twice Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 40, wherein at least one of said protein fragments comprises a tissue tropism determining fragment of a fiber protein ~~from~~ of a subgroup B adenovirus origin.

43. Canceled.

44. (Twice Amended) A ~~gene delivery vehicle~~ recombinant adenovirus comprising:
a recombinant virus capsid comprising protein fragments from at least two different viruses;

wherein said recombinant virus capsid has an increased tissue tropism for endothelial cells when compared to other gene delivery vehicles adenovirus capsids, ~~wherein said tissue tropism is being provided by a virus capsid and wherein said virus capsid comprises protein fragments from at least two different viruses.~~

45. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 44, wherein at least one of said at least two different viruses is an adenovirus.

46. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim ~~44~~ 45, wherein ~~at least one of said viruses~~ said adenovirus is a subgroup B adenovirus.

47. (Twice Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 44, wherein at least one of said protein fragments comprises a tissue tropism determining fragment of a fiber protein of subgroup B adenovirus origin.

48. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim ~~44~~ 46, wherein said subgroup B adenovirus is adenovirus 16.

49. (Twice Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 44, wherein said protein fragments are ~~not from an adenovirus of subgroup B and are~~ of adenovirus of subgroup C origin.

50. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 44, ~~wherein said virus capsid comprises protein fragments from at least two different viruses and wherein at least one of said protein fragments are not from an adenovirus of subgroup B and are~~ from an of adenovirus of subgroup C origin.

51. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 44, ~~wherein~~ further comprising an adenoviral nucleic acid incorporated within said recombinant virus capsid.

52. (Twice Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 51, wherein said adenoviral nucleic acid comprises sequences from at least two different adenoviruses.

53. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 51, wherein said adenoviral nucleic acid comprises at least one sequence encoding a fiber protein ~~comprising~~ having a tissue tropism determining fragment of a subgroup B adenovirus fiber protein.

54. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 51, wherein said adenoviral nucleic acid is modified such that the capacity of said adenoviral nucleic acid to replicate in a target cell has been reduced or disabled.

55. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 44, ~~further comprising~~ wherein said recombinant adenovirus is a minimal adenovirus vector or an Ad/AAV ~~ehimaerie~~ chimeric vector.

56. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 44, further comprising at least one non-adenoviral nucleic acid incorporated into said recombinant virus capsid.

57. (Amended) The ~~gene delivery vehicle~~ recombinant adenovirus of claim 56, wherein at least one of said non-adenoviral nucleic acids is a gene encoding a protein selected from the group of ~~genes encoding a protein selected from the group~~ proteins consisting of: an apolipoprotein, a nitric oxide synthase, a herpes simplex virus thymidine kinase, an interleukin-3, an interleukin-1 α , an (anti) angiogenesis protein, an anti-angiogenesis protein, an anti-proliferation protein, a smooth muscle cell anti-migration protein, a vascular endothelial growth factor (VEGF), a basic fibroblast growth factor, a hypoxia inducible factor 1 α (~~HIF-1 α~~) and a PAI-1.

58. (Amended) ~~An~~ A recombinant adenovirus capsid comprising:
~~having an increased tissue tropism for endothelial cells when compared to other adenovirus capsids, wherein said capsid comprises~~ proteins from at least two different adenoviruses; and
~~wherein~~ at least a tissue tropism determining fragment of a fiber protein is of subgroup B adenovirus origin.

Please add the following new claims:

59. (New) The recombinant adenovirus of claim 47, wherein said subgroup B adenovirus is adenovirus 16.

60. (New) A recombinant adenovirus having a capsid with a reduced tropism for liver cells and an increased tropism for smooth muscle cells and endothelial cells comprising:
a chimeric fiber protein comprising at least the knob domain of a fiber protein of adenovirus serotype 16;
wherein the remaining part of the fiber protein is of a different adenovirus serotype.

61. (New) The recombinant adenovirus of claim 60, further comprising an adenoviral nucleic acid incorporated within the capsid.

62. (New) The recombinant adenovirus of claim 61, wherein said adenoviral nucleic acid comprises a sequence encoding the chimeric fiber protein.

63. (New) The recombinant adenovirus of claim 60, wherein said recombinant adenovirus is a minimal adenovirus or an Ad/AAV chimeric vector.

64. (New) The recombinant adenovirus of claim 60, wherein said different adenovirus serotype is an adenovirus serotype of subgroup C.

65. (New) The recombinant adenovirus of claim 64, wherein said adenovirus of subgroup C is adenovirus serotype 5.

66. (New) A cell for producing a recombinant adenovirus having a tissue tropism for smooth muscle cells, said cell comprising:

means for assembling the recombinant adenovirus;

wherein said means comprises at least one adenoviral nucleic acid encoding a chimeric adenoviral fiber protein having at least a knob domain of a fiber protein of adenovirus serotype 16; and wherein the remaining part of the fiber protein is of a different adenovirus serotype; and

wherein said cell is of a PER.C6 cell (ECACC deposit number 96022940) origin.

67. (New) The cell of claim 66, wherein said different adenovirus serotype is an adenovirus of subgroup C.

68. (New) The cell of claim 67, wherein said adenovirus of subgroup C is adenovirus serotype 5.

69. (New) A recombinant adenovirus capsid having a reduced tropism for liver cells comprising:

a chimeric fiber protein comprising at least the knob domain of a fiber protein of adenovirus serotype 16;

wherein the remaining part of the fiber protein is of a different adenovirus serotype.

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70. (New) The adenovirus capsid of claim 69, wherein said different adenovirus serotype is an adenovirus serotype of subgroup C.

71. (New) The adenovirus capsid of claim 70, wherein said adenovirus of subgroup C is adenovirus serotype 5.
